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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,564	12/15/2005	John De Koning	67670-5004-US	2650

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EXAMINER
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CRANE, LAWRENCE E

ART UNIT	PAPER NUMBER
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1623

MAIL DATE	DELIVERY MODE
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03/24/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/517,564	<b>Applicant(s)</b> DE KONING ET AL.	
	<b>Examiner</b> Lawrence E. Crane	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on December 23, 2009 (Election).
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-30,32,33,35 and 37-66 is/are pending in the application.
- 4a) Of the above claim(s) 23-28 and 56-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-22,29,30,32,33,35,37-55 and 62-66 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 December 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/15/2007</u> .  | 6) <input type="checkbox"/> Other: _____                          |

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Examiner notes that the chemical structures in Figure 1 are noted to be legible, but that the names provided beneath said structures are in a font too small to be easily read and appear to be somewhat fuzzy. Substitution of drawings wherein this problem has been corrected is respectfully suggested.

Claims **3, 31, 34 and 36** have been previously cancelled, claims **23-28 and 56-61** have been withdrawn from consideration, claims **1, 15-18, 22, 33, 48-51, 55 and 62-65** have been amended, the disclosure has not been further amended, and no new claims have been added as per the amendment filed December 23, 2009. No additional or supplemental Information Disclosure Statements (IDSs) has been filed as of the date of this Office action. However, the English language abstracts provided, while helpful, are incomplete because each abstract has failed to provide a generic chemical formula to permit determination of the subject matter actually disclosed by the complete document. Therefore, examiner respectfully requests that, aside from documents already made of record by examiner herein, all other Japanese patent applications, NPL-type references, and patents cited in abstract form herein should be provided by applicant as a complete document and cited as of record on a new PTO-1449.

Claims **1, 2, 4-30, 32, 33, 35 and 37-65** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line **y**, the line number “y” is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **23-28 and 56-61** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, are withdrawn from further consideration by the examiner, 37 C.F.R. §1.142(b), as being drawn to a non-elected Invention (Group **II**). Election was made without traverse in Paper No. **20091223** (Election).

Applicant's election of Group **I**, claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, in Paper No. **20091223** is acknowledged. Because applicant did not distinctly and specifically point out the

supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a))

The application contains claims **23-28 and 56-61** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, are drawn to an invention non-elected without traverse in Paper No. **20091223**. A complete response to a subsequent final rejection must include cancellation of non-elected claims or other appropriate action (37 C.F.R. §1.144) MPEP §8.21.01.

The requirement is still deemed proper and is therefore made FINAL.

Claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, remain under examination in the case.

Claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, is/are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to consider in this analysis:

a) Actual Reduction to Practice? Inspection of the extensive listing of specific embodiments and the listings of names in, for example claim **22**, defines generic classes of DNA-type cAMP molecules always further modified by an 8-substituent and of similarly modified RNA-type cAMP molecules wherein additionally the 2'-hydroxyl has uniformly been modified by either O-methylation or N,N-dimethylcarbamoylation. However, the specific embodiments do not provide an adequate basis for extrapolation to cAMP analogues wherein the laundry lists of substituents groups, for example the compounds included within the definitions of substituent variables R<sub>1</sub>-R<sub>5</sub> or the compounds included by the generic term "dideaza-analogues and deaza-analogues" at line 3 of claim **1**. In addition examiner notes in particular the assertion of alternatives wherein selenium-containing substituents are included (very likely to be poisonous) and wherein the generic substituent "silyl" is listed, an assertion that suggests that SiH<sub>3</sub> groups may be included as substituents, an unlikely prospect in view of the fact that hydrogen-substituted silanes are well known to be pyrophoric (spontaneously

flammable in air). Examiner respectfully suggests that the instant generic claims need to be limited to subject matter that is possibly operative, at least by deletion of subject matter that is obviously inoperative.

b) Disclosure of Drawings or Structural Chemical Formulas? This factor is not important to this particular analysis.

c) Sufficient relevant identifying characteristics? This factor has been dealt with in a previous paragraph.

d) Method of making the claimed invention? The synthesis of specific embodiments within the instant disclosed embodiments is well described in synthetic examples, but there are no examples wherein the successful synthesis of silyl- or selenium-substituted cAMP compounds has been disclosed, or wherein the administration of such compounds for the treatment of any disease condition has been disclosed or otherwise exemplified, including those disease conditions described generically (e.g. "cancer") and specifically (e.g. "diabetes") in claims **62-65**.

e) Level of skill in the art? This factor is not important in this particular analysis.

f) Predictability in the art? The treatment of "cancer" remains unpredictable, particularly in regards neoplasms of the nervous system and of organs including for example neoplasms of the liver and the pancreas. Also, while there exist treatments of diabetes, the disease remains incompletely understood and therefore methods directed to the effective treatment thereof remain somewhat unpredictable as well, in the absence of a clear showing of effective results. No clearly applicable test results supporting the effective treatment of any disease condition have been provided thus far within the file record of this application.

For the above reasons, the instant claims are found to lack adequate support from the written description. Examiner respectfully suggests deletion of inoperative and unlikely to be operative subject matter from the claims and/or the submission of additional test results and synthesis data to provide the written description necessary to support a broader scope of claimed subject matter.

Claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the synthesis of a limited number of RNA-type and DNA-type cAMP analogues and pharmaceutical compositions thereof, does not reasonably provide enablement for the vast array of compounds, pharmaceutical compositions and methods of disease treatment encompassed by the instant claims as presently in the case. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of “undue experimentation” is appropriate are as follows:

The analysis in the previous rejection presently if found to also provide an adequate basis in support of a finding of inadequate enablement. Therefore, applicant is referred to the analysis above as being equivalent to the Wands analysis normally presented herein.

Claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, are objected to because of the following informalities:

In claim **1** there are numerous typographical errors *in re* the representation of variable substituent groups; e.g. variables “**R1**” and “**R3**” are shown as displayed in the generic chemical structure at line 2, but are listed as :”**R<sub>1</sub>**” and “**R<sub>3</sub>**” in subsequent definitional paragraphs. There are many other such inconsistencies in this and subsequent claims. Correction of all such inconsistent displays of definitional variables is respectfully requested with the substitution of subscripts for all such variables suggested as the best alternative.

Appropriate correction is required.

Claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, are rejected under 35 U.S.C. §112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, there are included listing of possible substituent groups, but said listings are frequently lacking in an appropriate Markush format or the term -- or -- between the last two members of what appears to be listings of alternative substituent groups. Therefore, in each of these listings that defines a single variable substituent, applicant has advanced claims that include major valence errors because carbon can only have a maximum valence of 4 in compounds of the kind claimed herein. Appropriate correction to make clear the alternative nature of each and every such listing is respectfully requested.

In claim **1** at line 19, the term “esters and/or solvates” is indefinite because the particular substances being referred to have not been defined. Deletion or other appropriate action is respectfully requested. See also claim **33** wherein the same problem reoccurs.

In claim **1** at line 20, the term “with the exception of ... [listing of names]” appears to be a --proviso --. Applicant is respectfully requested to substitute for the noted term -- with the proviso that the following named compounds are excluded: --. See also independent claim **33** wherein this proviso/”exception” is not present, and wherein the absence of this limitation supports the rejections above alleging lack of written description and lack of enablement.

In claim **1** at line 4, the term “azido” is outside of the metes and bonds of elected subject matter, because the C-6 substituent renders the generic class of compounds being claimed no longer a cAMP-type compound. See also claim **33** wherein the same problem occurs and wherein the term “S-aryl” in the definition of variable R<sub>3</sub> is also outside of the genus elected. Deletion of the noted terms from both claims is respectfully requested.

Claims **29 and 30** are improperly dependent for failure to further limit the subject matter of a compound claim. The sole limitations presented in the noted claims are -- method of treatment -- limitations and therefore have no patentable weight in a compound claim. Cancellation is respectfully requested.

In claim **33** at line 1, the term “method for treating a patient” is incomplete because no disease to be treated has been specified, effectively reducing the instant claim and most claims

dependent therefrom to the status of a compound claim, and in addition rendering determination of the metes and bounds indeterminate. Said term also renders the claim incomplete because the term "patient" is incomplete; said term should be amended to read | -- patient in need thereof --.

In claim **48**, if claim **33** is amended as suggested, this claim may no longer be properly dependent for failure to further limit.

In claim **65**, the term "a human disease" is incomplete because the specific disease or diseases to be treated has/have not been specified with particularity.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(c) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **16-19, 52 and 55** and linking claims **1, 2, 4-15, 20-22, 29, 30, 32, 33, 35, 37-51, 53, 54 and 62-66**, to the degree applicable, are rejected under 35 U.S.C. §102(b) as being anticipated by **Kataoka et al. '792** (PTO-1449 ref. **C2**; abstract of **JP 11130792**) wherein the Japanese application document (PTO-892 ref. **L**) is referenced in addition to permit understanding of the intended meanings of the variables defined in the abstract wherein no generic chemical structure has been provided.



The disclosure in the abstract is sufficient to determine that the compounds, pharmaceutical compositions and methods of treatment claimed herein have been anticipated by the cited reference in view of the generic structure found at the bottom of column 1 of the first page of the actual Japanese language reference (PTO-892 ref. L).

Claims **16-19** and linking claims **1, 2, 4-15, 20-22, 29, 30 and 32**, to the degree applicable, are rejected under 35 U.S.C. §102(b) as being anticipated by **Weimann et al. '885** (PTO-892 ref. A).

Applicant is referred to the Abstract of the **'885** reference wherein compounds claimed herein have been anticipated.

Claims **16-19** and linking claims **1, 2, 4-15, 20-22, 29, 30 and 32**, to the degree applicable, are rejected under 35 U.S.C. §102(b) as being anticipated by **Sopchik et al.**(PTO-892 ref. U).

Applicant is referred to page 5912, column 2, the compounds labeled “cis-13” and “cis-14” as anticipating the instant claimed subject matter.

Claims **16-19** and linking claims **1, 2, 4-15, 20-22, 29, 30 and 32**, to the degree applicable, are rejected under 35 U.S.C. §102(b) as being anticipated by **Kataoka et al.** (PTO-892 ref. V).

Applicant is referred to page 1597, column 1, the listing of compounds “3a-d,” all of which anticipate the instant claimed subject matter.

Claims **16-19** and linking claims **1, 2, 4-15, 20-22, 29, 30 and 32**, to the degree applicable, are rejected under 35 U.S.C. §102(b) as being anticipated by **Ikehara** (PTO-892 ref. W).

Applicant is referred to page 81 wherein the compound labeled “3” anticipates the instant claimed subject matter.

Claims **16-19** and linking claims **1, 2, 4-15, 20-22, 29, 30 and 32**, to the degree applicable, are rejected under 35 U.S.C. §102(b) as being anticipated by **Gulyeav et al.** (PTO-892 ref. X).

Applicant is referred to the circled structure at page 2 of the Abstract, a structure (has a 2'-azido substituent) that anticipates the instant claimed subject matter.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < <http://pair-direct.uspto.gov> >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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**03/20/2010**

/Lawrence E. Crane/

Primary Examiner, Art Unit 1623

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